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Use of excess mortality from respiratory diseases in the study of influenza*

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Since 1970, WHO has conducted a collaborative study on the use of "excess mortality" from respiratory diseases (that is, the number of deaths actually recorded in excess of the number expected on the basis of past seasonal experience) in order to assess in 13 different countries the severity of influenza epidemics. The use of computer-produced seasonal expected and actual curves permits quick visual assessment of influenza activity in any one country, as well as comparisons between different countries. The study demonstrates that an excess in the observed over the expected number of total deaths does not necessarily indicate an excess in deaths from influenza, and it is therefore limited, at least for the present time, to deaths from respiratory disease. It provides a week-to-week record of deaths from acute respiratory disease in countries where weekly returns are available and a retrospective analysis of the disease pattern in the collaborating countries. This study will be continued for a number of years and, apart from its value to the individual countries, should provide useful comparisons between countries with different climates.

The main aim of the Influenza Programme established in 1947 by the World Health Organization is to obtain, as rapidly as possible, strains from cases or outbreaks of influenza in any part of the world in order to determine by quick and careful examination, their characteristics and similarity in relation to previously identified strains. Its second objective is to collect and distribute as much epidemiological information as it is possible to obtain from national authorities.

In contrast to the precise information obtained about viruses, the quantity and quality of the epidemiological information varies. Influenza is not a notifiable disease in most countries, and even in highly developed countries morbidity returns from general practitioners and hospitals are not usually published except during epidemics. Data on industrial and school absenteeism provide useful information during epidemic periods, but these data are not normally available in many countries. Furthermore, sickness benefit claims are limited to the working population and do not, therefore, reflect the disease picture in the total population.

In the USA and a few other countries with temperate climates, the "excess mortality" from all acute respiratory diseases (i.e., the number of deaths actually recorded in excess of the number expected on the basis of past seasonal experience) has been shown to be a useful method for assessing the severity of influenza epidemics (1–3). These mortality statistics are readily available, at least to some administrative divisions in many countries, during and between epidemics.

Since 1970, WHO has been conducting a collaborative study on the use of "excess mortality" from respiratory diseases. Thirteen countries (Table 1) with different climates, situated in different parts of the world, are providing the necessary statistical information. At WHO headquarters, a computer has been programmed to construct seasonal mortality curves that are expected in the light of data from a preceding period of 5–10 years. Data from Mexico and Panama are not included in this report because information for 1973 is not yet available. Data from Japan were received while the report was in preparation and the expected seasonal curve could not be included in Fig. 2.

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Table 1. List of countries in the WHO collaborative study on the use of excess mortality from respiratory diseases in the study of influenza

	Information available since:
Czechoslovakia (Czech republics)	1963/64
Denmark (Copenhagen)	1963/64
England and Wales	1963/64
Hong Kong	1965/66
Israel	1965/66
Japan	1963/64
Lebanon (Beirut)	1967/68
Mexico	1963/64
Netherlands	1963/64
Panama	1963/64
Scotland	1964/65
USA (122 cities)	1963/64
USSR (30 cities)	1966/67

METHODS

The respiratory diseases included in the study are listed in the accompanying tabulation.

Disease	*ICD category (4)*	
	1955 Revision	*1965 Revision*
influenza	480-3	470-4
pneumonia	490-3	480-6
bronchitis	500-2	466, 490-3

Because the USA and Israel do not report deaths from bronchitis, and because these data have been available for the USSR only since 1970, only deaths from influenza and pneumonia in these three countries were included in the study.

In general, a report covers an entire country but sometimes only a part of a country is covered. The reports from Czechoslovakia cover only the Czech republics, those from Denmark only Copenhagen, and those from the Lebanon only Beirut, while those from the USSR cover 30 cities and those from the USA 122 cities.

In 1970, the countries participating were requested to provide retrospective data on mortality from respiratory diseases for the preceding 5–10 years in terms of weekly records whenever available, otherwise as numbers of deaths per month. Great Britain (England and Wales and Scotland), Israel, and the USA furnished weekly records and have continued to report weekly. Czechoslovakia and Denmark provided retrospective monthly data, but Czechoslovakia has been reporting weekly since 1971 and Denmark since 1972. For all the other countries, only monthly data were available. In processing the data the weekly returns were grouped into periods of 4 weeks, while the monthly records were processed as such.[1] The data bank is revised every year by incorporating the information for the preceding 13 four-week periods (or 12 months) and by excluding the corresponding earliest information that was used previously.

Up to the end of 1972, data were processed for full calendar years, i.e., January to December, but starting in 1973 the " epidemic year " was adopted instead. The latter is assumed to be the period of 12 months between 1 April and 31 March. The expected seasonal curves incorporating the experience of the previous winter can now, therefore, be available before the start of the next influenza season in the northern hemisphere.

The computer has been programmed to provide, in terms of numbers of deaths, the expected seasonal mortality from respiratory diseases. In computing the expected number of deaths an estimated secular trend is built in (5), based on the number of deaths occurring during the 4-week periods (or months) of low mortality.

To determine the expected seasonal variations, two sets of data are fed to the computer. The first set comprises deaths in the years of low mortality, during which no known sizeable outbreaks of influenza have occurred. The second set comprises deaths in all the years under study with the exception of those with very high peaks.

Two " expected " seasonal curves are therefore available, but experience has shown that the second seasonal curve, constructed from deaths in all the years under study except those in which very high peaks occurred, is entirely adequate for the comparisons. Apart from England and Wales, for which the two seasonal curves are given as an example (Table 2; Annex 1), only the second expected seasonal curves are given for the other countries in this report.

The observed data are plotted by computer up to the end of the twelfth week of the year (or the end of March). Information for the rest of the year, i.e., after March and for the following influenza season, is traced by hand. After revision of the data,

[1] In the case of Czechoslovakia and Denmark, data processing is continuing on a monthly basis until information has accumulated for 4–5 years.

Table 2. Observed and expected deaths from influenza, pneumonia and bronchitis in England and Wales during the "influenza season", October–March, over the period 1963/64–1972/73

Influenza season (October–March)	Observed	Expected I [a]		Expected II [b]	
		number	excess [c]	number	excess [c]
1963/64	37 272	35 100	2 172	37 617	(345)
1964/65	35 113	35 768	(655)	38 285	(3 173)
1965/66	47 153	36 438	10 715	38 954	8 199
1966/67	33 756	37 105	(3 349)	39 623	(5 867)
1967/68	54 670	37 776	16 894	40 290	14 380
1968/69	42 431	38 443	3 988	40 959	1 472
1969/70	64 882	39 113	25 769	41 628	23 254
1970/71	38 945	39 781	(836)	42 297	(3 352)
1971/72	44 326	40 449	3 877	42 894	1 432
1972/73	50 944	41 118	9 826	43 635	7 309

[a] Based on deaths in years where no known major influenza activity occurred, i.e. 1964/65, 1966/67 and 1970/71.

[b] Based on deaths in all years under study, but excluding those years with exceptionally high peaks, i.e. 1967/68, 1969/70 and 1972/73.

[c] Deficits are given in parentheses.

the graphs are distributed every year to the participants.

RESULTS

Deaths from respiratory diseases

Lowest number of deaths (Annexes 1 & 2). In Europe, Mexico, and the USA the number of deaths was usually lowest in August and September, but was also low in July. In Japan it was usually lowest in September, and in Israel in October. In Hong Kong it was almost always lowest in October. There was no definite pattern in the Lebanon, where the number of deaths may be lowest in any month between June and October; this could be the result of fluctuations in the small numbers involved (less than 10 deaths per month) rather than any seasonal influence. In Panama, on the other hand, the number of deaths was usually lowest in the period between April and June, probably owing to the seasonal pattern in tropical climates.

Highest number of deaths (Annexes 1 & 2). With the exception of Hong Kong, the number of deaths was usually highest in January and somewhat lower in December and February. In Hong Kong, the number of deaths was highest in March in 5 of the 7 years for which information is available. Furthermore, a high number of deaths was frequently observed during the summer months, particularly those of 1968. A high number of deaths during summer was also seen to a lesser extent in the Lebanon, but not in Israel.

Period from 1963/64 to 1967/68. The period under study, 1963–73, can be conveniently divided into two parts: one before and one after the advent of A/Hong Kong/1/68 (H3N2) virus. The experience, depicted by excess mortality from respiratory diseases (Annexes 1 & 2) up to the summer of 1968, is briefly as follows.

Except for Czechoslovakia and Denmark, the 1963/64 season was marked by a very small, if any, excess in mortality and, except for Japan and the USA, a similar picture was shown for the 1964/65 season.

Small to moderate excesses in mortality were seen in the 1965/66 season in all countries except Japan. The 1966/67 season was noted for its markedly lower-than-expected mortality for all countries, except Czechoslovakia, Hong Kong, and the USSR. In contrast, the winter of 1967–68 was marked by

large excesses with the exception of Hong Kong and the USSR.

The above picture tallies well with morbidity as reported in the annual reports of the Director-General of WHO, 1963–68 (6–11), and in the *Weekly Epidemiological Record*, 1965–69 (16–19), but it does not correlate with drifts in the haemagglutinin antigen of the influenzavirus A over the same period. The proportion of variants from the 1957 strain, which were first detected in 1961, increased progressively until 1964 when the variant A/England/12/64 (H2N2) completely replaced A/Singapore/1/57 (H2N2), the prototype virus (24). Further variants kept a close antigenic relationship to the A/England/12/64 strain. While the appearance of A/England/12/64 did not herald large outbreaks, there were during the winter of 1968 large outbreaks apparently caused by strains that were antigenically very close to the same variant.[1] Influenzavirus B played a minor role in deaths from respiratory disease during this period notwithstanding the appearance of variant B/Roma/1/67.

Period from 1968 onwards. The advent of A/Hong Kong/1/68 (H3N2) was marked by a very high mortality from respiratory diseases in Hong Kong during the summer of 1968. However, except for the USA, where deaths from respiratory infections were very heavy, the excess in deaths during the 1968/69 season was mild to moderate in the participating countries. In contrast, during the 1969/70 season mortality was mild in the USA but very high in all the other countries. The following season, 1970/71, was marked by low mortality from respiratory infections in all countries in the study. The 1971/72 season was noted for excess mortality but the experience of participating countries differed in magnitude. In the Lebanon and Israel the number of deaths was very high.

With the exception of the Lebanon, where deaths actually fell short of the figure expected, the 1972/73 season was, like the preceding one, marked by excess mortality whose magnitude again differed among the participating countries. The USSR reported a very large number of deaths. In Scotland a marked difference was noted between the observed and expected number of deaths during January 1973 only.

Again, the excess in mortality for this period tallies with morbidity and mortality as reported in the annual reports of the Director-General of WHO, 1968–72 (11–15), and in the *Weekly Epidemiological Record* 1970–73 (20–23).

With regard to the antigenic structure of influenzavirus A, the outbreaks and corresponding excess mortality in the 1968/69 and 1969/70 seasons were temporally associated with a shift from previous strains in the haemagglutinin of the A/Hong Kong/1/68 (H3N2) virus. In 1970/71, no further changes were apparent in the antigenic structure of influenzavirus A and, as noted above, there was low mortality from respiratory diseases.

In the 1971/72 season, a new variant of the influenzavirus A was recognized, A/Hong Kong/5/72 (H3N2), which showed a marked antigenic drift. However, except for Hong Kong and Japan, where the variant A/Hong Kong/5/72 was isolated in large numbers, the viruses identified during the 1971/72 outbreaks differed little from the original A/Hong Kong/1/68 virus.

In the 1972/73 season, the influenza outbreaks and the corresponding excess mortality from respiratory diseases were associated with a marked antigenic drift in the haemagglutinin and neuraminidase of the A/England/42/72 (H3N2) variant of the type A influenzavirus. This strain had completely taken over from both the A/Hong Kong/1/68 and A/Hong Kong/5/72 strains.

Again influenzavirus B hardly played a role but a new variant, B/Hong Kong/5/72, which was first isolated in December 1972 and January 1973, spread outside Hong Kong (and Australia) apparently too late in the season to cause serious outbreaks.

Total deaths from all causes

At a meeting of directors of the WHO respiratory virus and enterovirus reference centres in 1973, it was suggested that because a proportion of deaths from influenza may have been attributed to other causes, e.g., cardiac disease, an attempt should be made to study excess total mortality, in addition to excess deaths from respiratory diseases alone. For this purpose, figures for deaths from all causes in England and Wales, the Lebanon, Scotland, and the USA were processed in the same manner as the figures for deaths from respiratory diseases (Annex 3). Four-week periods (or months) of both low and peak total mortality were found to agree more or less with those noted for respiratory diseases, but troughs and peaks of total mortality tended to recur more frequently in the same four-week period or month each year.

[1] With the possible exception of A/Tokyo/3/67, which may have played a part in the 1967/68 influenza epidemics though it was not frequently isolated (25).

Table 3. Excesses and deficits [a] in numbers of deaths from respiratory infections and from all causes during influenza seasons

Influenza season	England and Wales [b]		Scotland		USA [c]		Lebanon	
	resp. inf.	all causes	resp. inf.	all causes	resp. inf.	all causes	resp. inf.	all causes
1964/65	(3 173)	(7 187)	75	514				
1965/66	8 199	17 253	668	1 319	482	(1 875)		
1966/67	(5 867)	(15 586)	(356)	(892)	(1 780)	(7 267)		
1967/68	14 380	27 143	303	1 057	861	5 350	8	107
1968/69	1 472	2 310	53	45	5 158	16 196	(3)	47
1969/70	23 254	20 082	532	898	578	6 213	0	(126)
1970/71	(3 352)	(6 553)	(337)	(873)	(913)	809	4	(33)
1971/72	1 432	7 603	207	251	554	1 153	13	110
1972/73	7 309	12 794	(2)	(69)	645	1 326	(8)	47

[a] Deficits are given in parentheses.
[b] No information is readily available for total deaths during the 1963/64 season.
[c] No information is available for total deaths for the 122 cities during the 1963/64 and 1964/65 seasons.

In England and Wales and in Scotland, the troughs and peaks of total mortality corresponded with those seen in deaths from respiratory disease. Except on one occasion, during the 1969/70 influenza season in England and Wales, the number of total deaths that exceeded or fell short of the expected number was greater than the corresponding number of deaths from respiratory disease (Table 3). In the 1969/70 season in England and Wales, however, the number of total deaths exceeded the expected number by 20 082, while those ascribed to respiratory diseases exceeded the expected number by 23 254. In a season when influenza outbreaks are known to have occurred, a larger excess of deaths from all causes compared with that for deaths from respiratory diseases might support the assumption that some cases of mortality from influenza were attributed to diseases other than respiratory infections. This assumption does not provide an explanation for a greater " deficit " in deaths from all causes in seasons with minimal influenza activity. Furthermore, the larger excess in deaths from respiratory diseases during the 1969/70 season in England and Wales is against the assumption of a frequent misdiagnosis of influenza, unless deaths from other causes had been attributed to respiratory infections.

In the USA, excesses and deficits in total deaths did not always tally with those of deaths from respiratory diseases. The most marked discrepancies occurred in 1965/66 when deaths from respiratory diseases exceeded the expected number by 482, and the total deaths fell short by 1 875. The reverse was seen in 1970/71, when, in conformity with the epidemiological picture, deaths from respiratory diseases fell short of the expected number by 913, but total deaths exceeded the expected number by 809 (Table 3).

In contrast to Annexes 1 & 2, the graphic record of excess total deaths is dwarfed in Annex 3 for England and Wales, Scotland, and the USA. For example, the excess deaths in England and Wales and Scotland during the large outbreaks of A/Hong Kong/1/68 (H3N2) influenzavirus in 1969/70, and in the USA in 1968/69, accounted for only a small proportion of the expected number of total deaths, as indicated also by the data in the accompanying tabulation.

	Excess deaths (%) from: Respiratory disease	Total mortality
England & Wales	55.9	7.0
Scotland	29.6	5.8
USA	38.0	5.1

In the Lebanon, the winter peaks of deaths from respiratory disease do not agree with those for total deaths, except in 1971/72, when a very large outbreak of influenza occurred (Annexes 2 & 3). Similarly, the proportions of excess deaths from respiratory disease do not agree with those for total mortality;

during the summer of 1968 (April to September), for example, the excess deaths from respiratory infections amounted to 31.0% of the expected number and those of total mortality to only 1.8%.

DISCUSSION AND CONCLUSION

Although the choice of mortality figures for depicting influenza activity quantitatively is admittedly somewhat crude, it would seem, in the absence of more accurate quantitative clinical data that excess mortality from respiratory disease is still useful in epidemiological studies.

The use of seasonal expected curves permits quick visual assessment of influenza activity and, furthermore, the charts are drawn to different scales to facilitate immediate comparison of influenza activity in different countries, irrespective of large differences in the actual numbers of deaths.

It is recognized that a high peak during one four-week period or month may, if care is not taken in reading the charts, overshadow a larger excess sustained during several periods at a lower level.

It has been stated that excess total mortality may provide a better indication of the magnitude of influenza outbreaks (1). While it is recognized that influenza may cause more deaths than those so certified, the opposite could also be true, though presumably to a lesser extent (2). Thus, deaths from other causes, e.g. coronary heart disease, may also be correlated with the cold winter weather (26). Whatever the reasons may be, some discrepancies have been noted in the present study between deaths from respiratory disease and total deaths. Moreover, though dealing with absolute numbers, the use of graphs limits the analysis of information to a visual comparison of the relative rise of observed deaths above the expected curves. Considering the much higher number of deaths from all causes than from respiratory diseases, deviations from the expected base-line are, of necessity, proportionately smaller, thereby reducing the effectiveness of the graphic presentation especially in cases of mild or moderate excesses.

In warmer climates, represented in this study by the Lebanon, other factors than influenza presumably also play a part in total deaths. It would, therefore, seem advisable to limit the study, at present, to deaths from respiratory infections only.

Meanwhile, this inquiry is providing a week-to-week record of deaths from acute respiratory diseases in countries where weekly returns are available, and a retrospective analysis of the disease pattern in the collaborating countries. It will be continued for a number of years and in addition to its value to individual countries in the scheme, it may provide useful comparisons between countries with different climates.

ACKNOWLEDGEMENTS

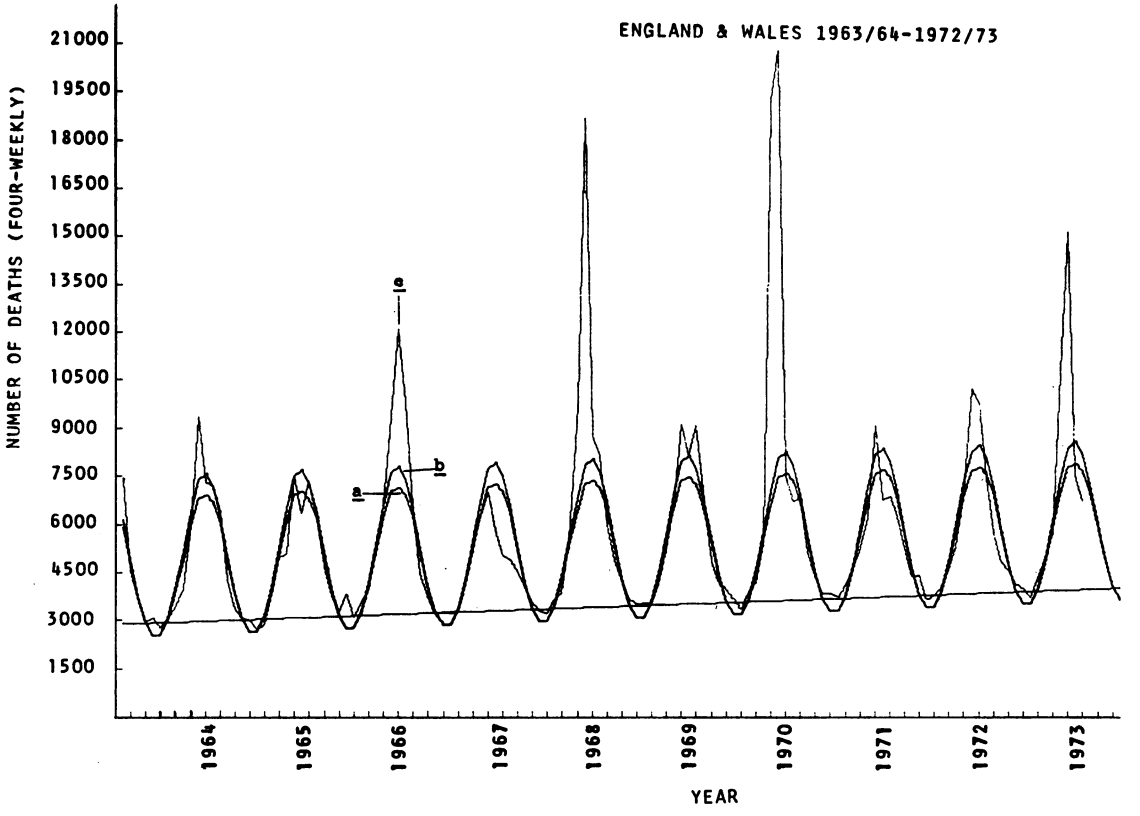
The authors gratefully acknowledge the cooperation of the participants from the countries in Table 1 in providing the data used in this paper.

Annex 1

DEATHS FROM INFLUENZA, PNEUMONIA, AND BRONCHITIS IN ENGLAND & WALES, 1963/64–1972/73

The 3 curves, plotted by the computer, represent during periods of 4 weeks: (*a*) the expected seasonal curve constructed from deaths in the years of low mortality when no sizeable outbreaks of influenza occurred, (*b*) the expected seasonal curve based on deaths in all the years under study except those in which very high peaks occurred, and (*c*) the curve of actual numbers of deaths.

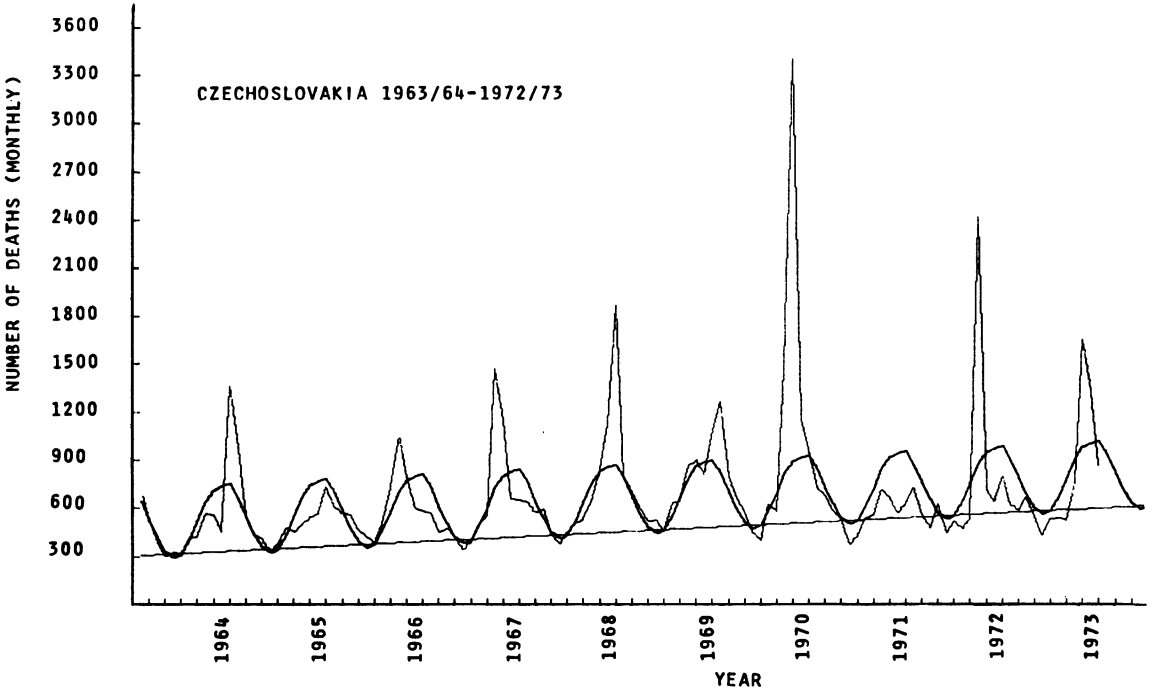
Annex 1 (continued)

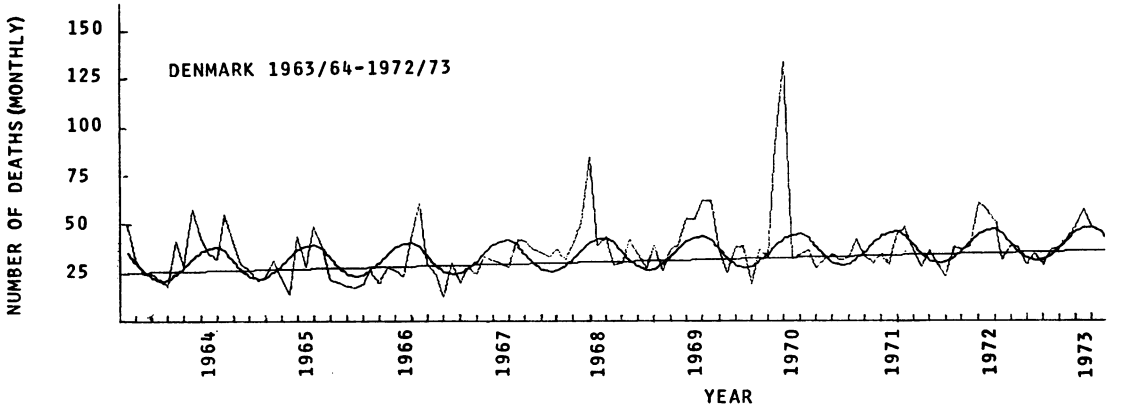


Annex 2

DEATHS FROM RESPIRATORY DISEASES IN CZECHOSLOVAKIA, DENMARK, HONG KONG, ISRAEL, LEBANON, NETHERLANDS, SCOTLAND, USA, AND THE USSR

These curves were plotted by the computer on figures for the actual and expected seasonal numbers of deaths from influenza, pneumonia, and bronchitis in all these countries, except Israel, the USA, and the USSR where they refer to influenza and pneumonia deaths only. For the Netherlands, two curves are presented because the troughs of the observed seasonal data for the period 1963/64–1972/73 were seen to take a higher value beginning in 1969, the year in which the Eighth Revision of the ICD (1965) was adopted. An expected seasonal curve based on information gathered from 1969 onwards was therefore constructed. No similar observation was made in the other countries.





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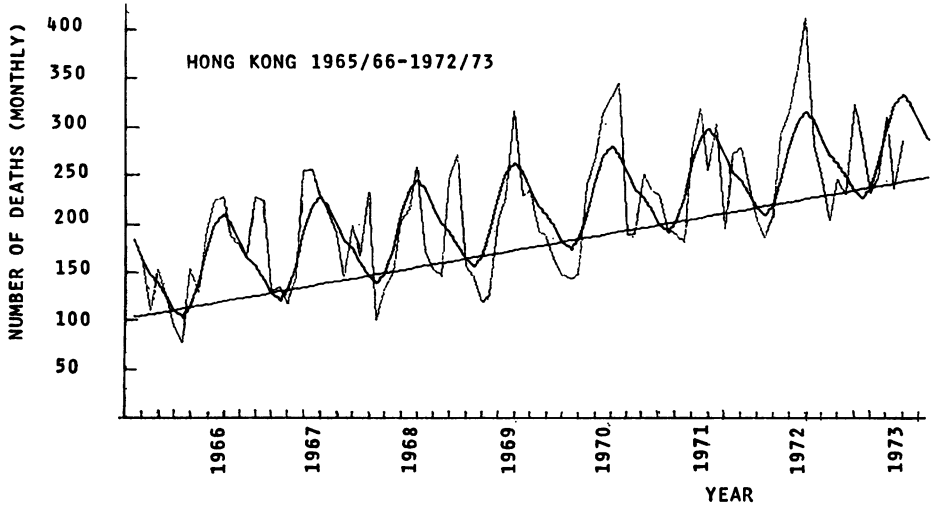

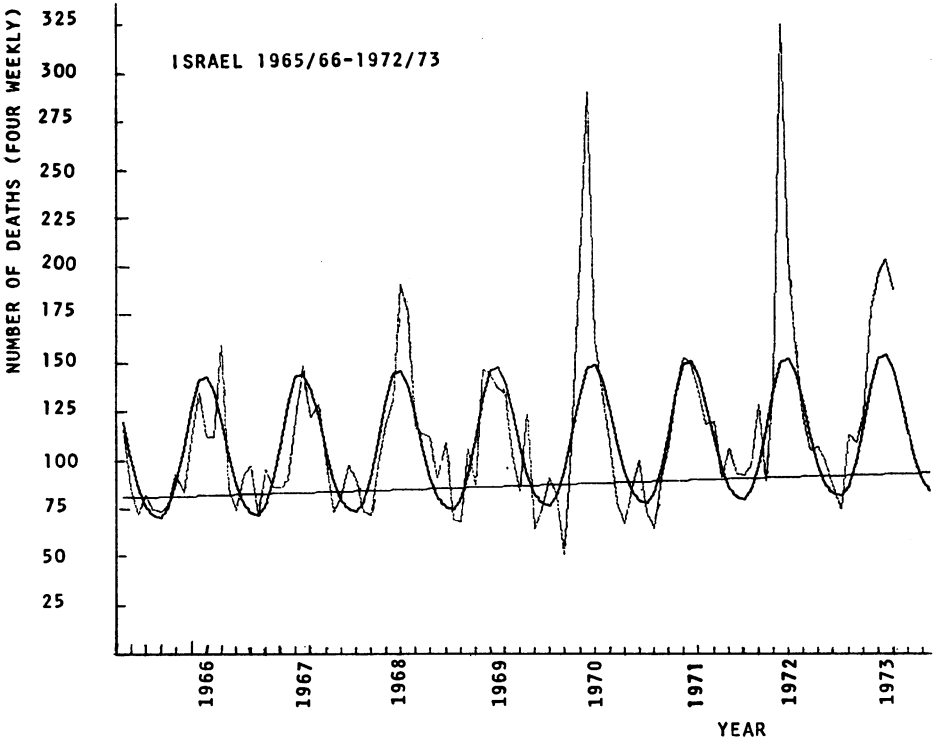

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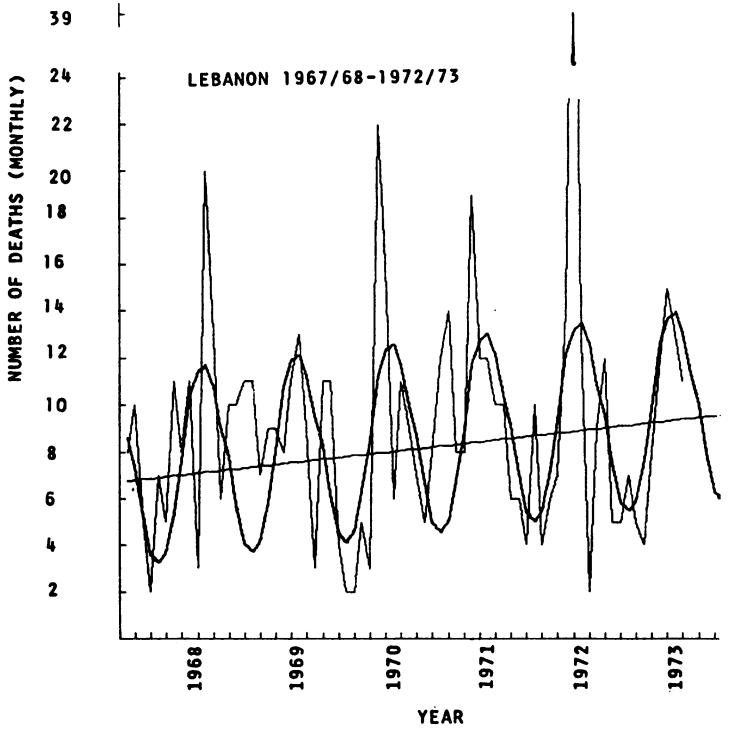

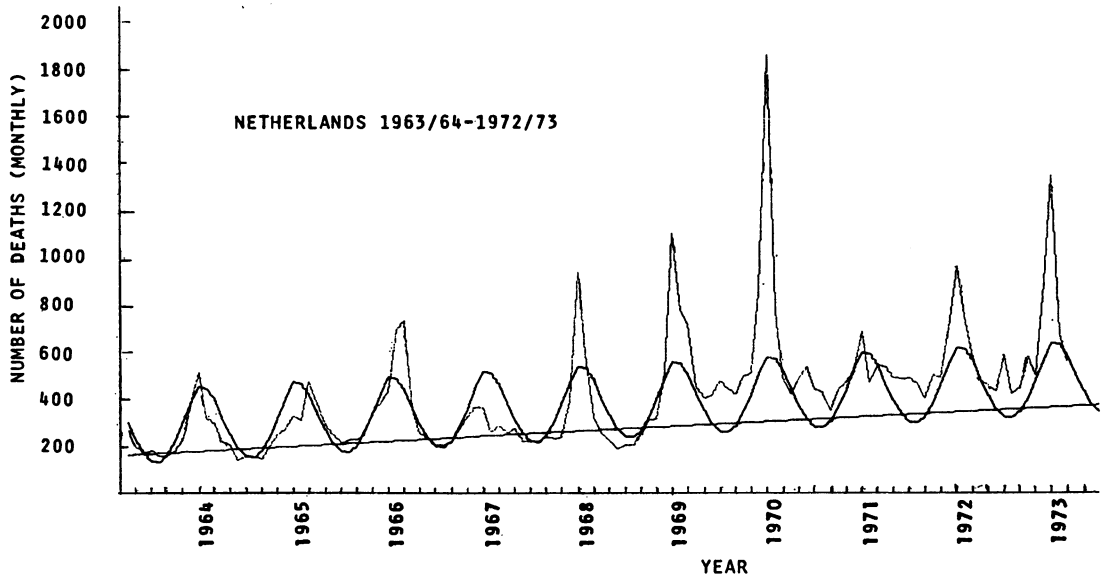

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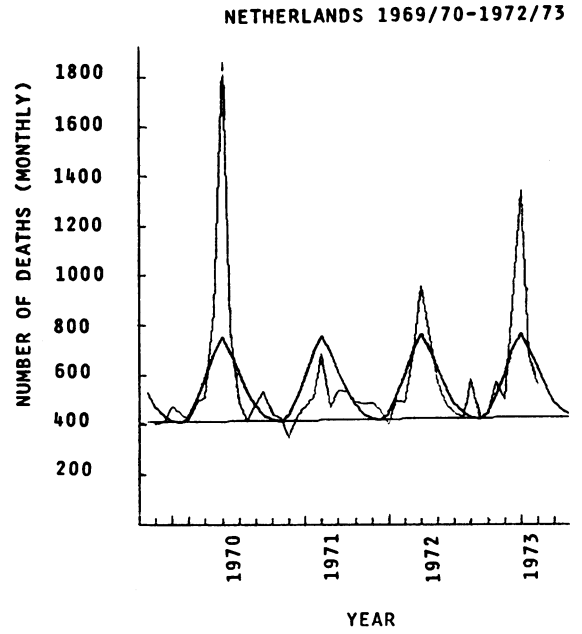

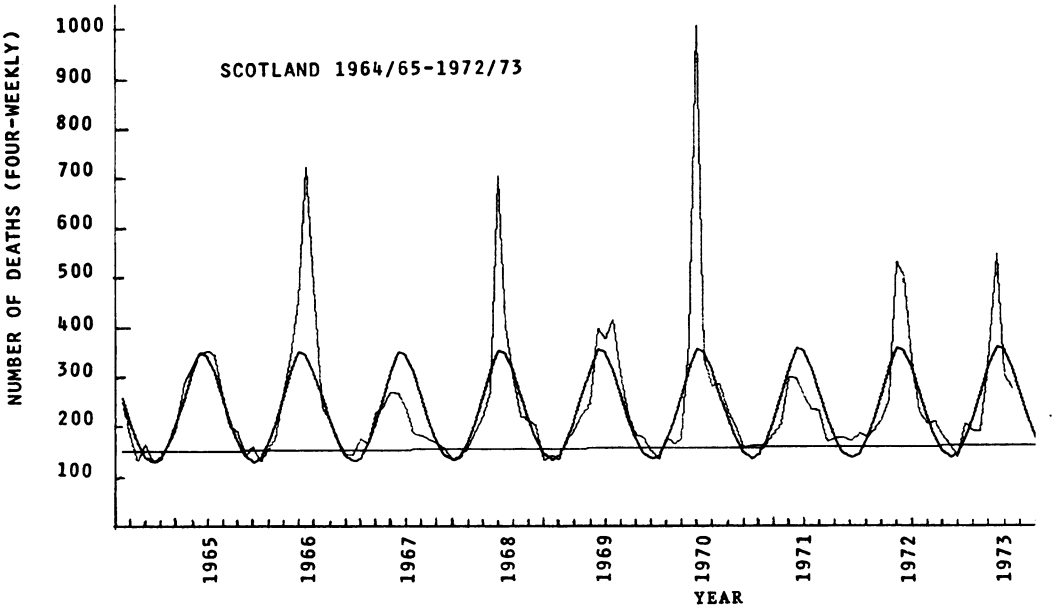

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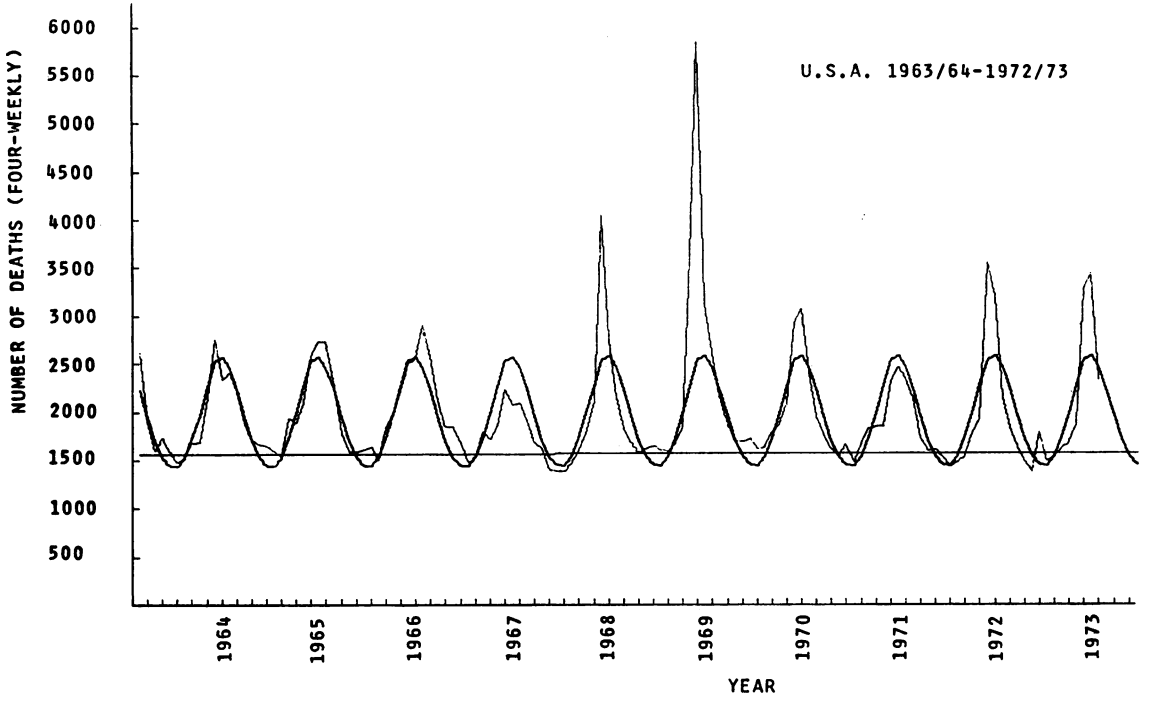
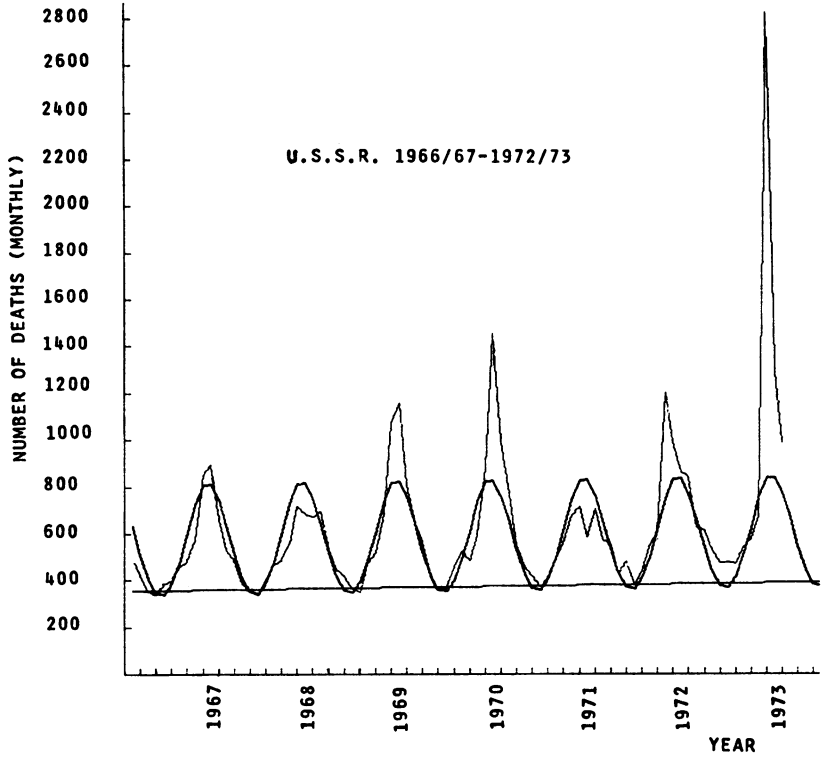
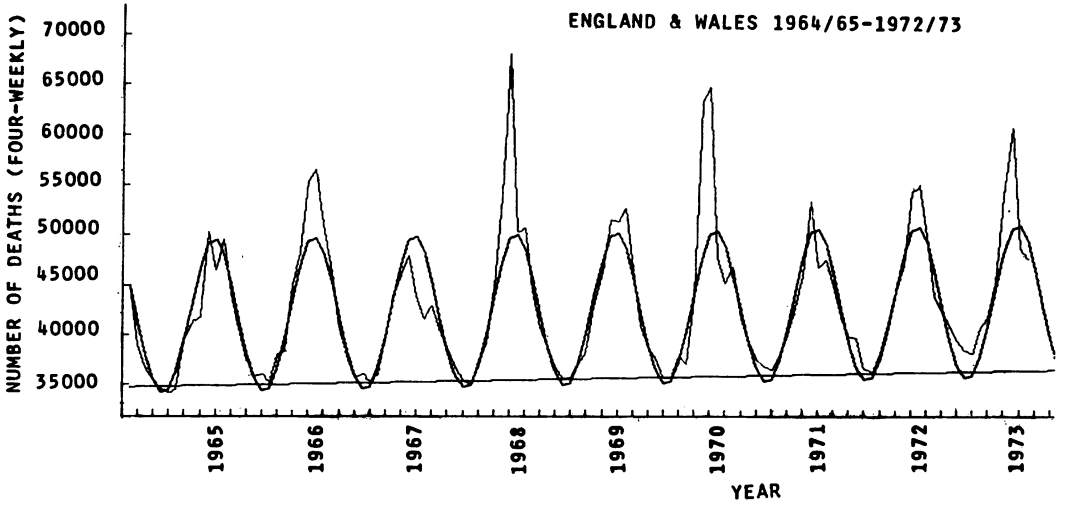


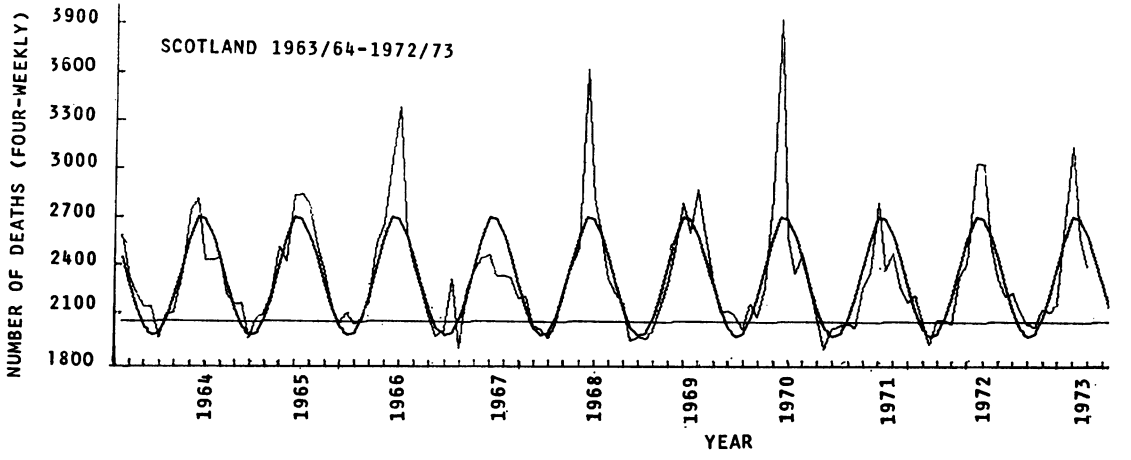


Annex 3

DEATHS FROM ALL CAUSES (TOTAL DEATHS) IN GREAT BRITAIN (ENGLAND & WALES, AND SCOTLAND), LEBANON, AND THE USA

The curves here represent the actual and expected seasonal deaths from all causes.





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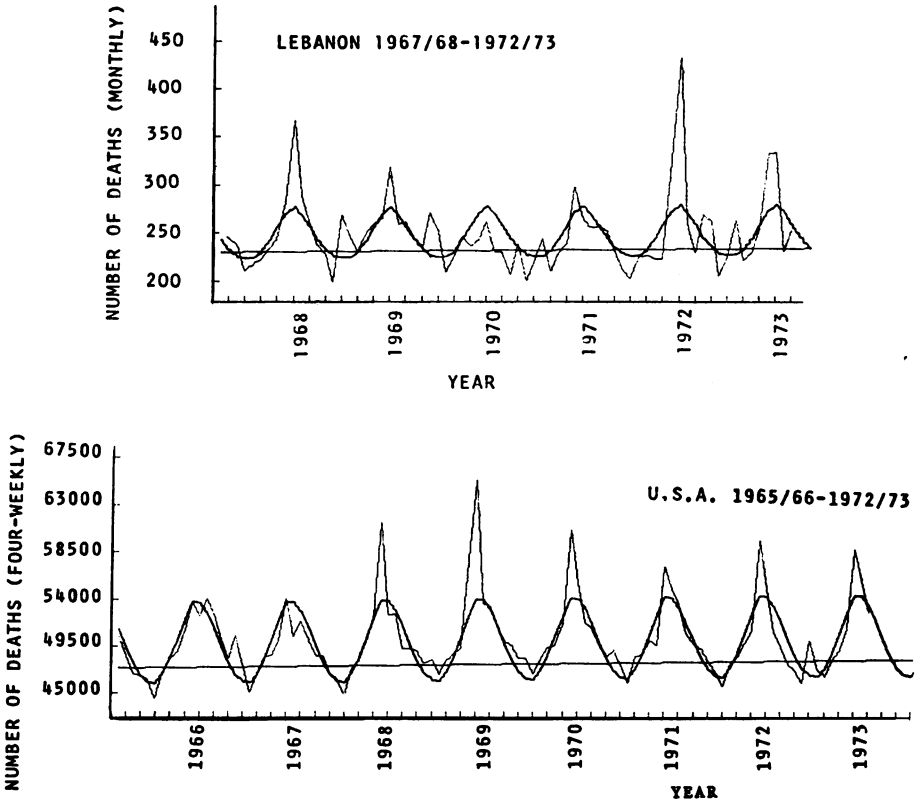

RÉSUMÉ

UTILISATION DE LA SURMORTALITÉ CAUSÉE PAR LES MALADIES RESPIRATOIRES POUR L'ÉTUDE DE LA GRIPPE

Contrastant avec les informations précises obtenues au sujet des virus grippaux, les données épidémiologiques relatives à la grippe sont de volume et de qualité variables. Une méthode pratique et généralement utile pour évaluer la gravité des épidémies grippales consiste à déterminer la surmortalité due aux maladies respiratoires, c'est-à-dire le nombre de décès enregistrés excédant le nombre escompté en se basant sur les statistiques saisonnières antérieures.

Depuis 1970, l'OMS mène une étude collective sur l'utilisation des chiffres de la surmortalité causée par les maladies respiratoires. Treize pays, aux climats différents et situés dans diverses parties du monde, fournissent les informations indispensables. Un programme sur ordinateur a été conçu au Siège de l'Organisation afin d'établir les courbes de la mortalité saisonnière prévue en fonction des données recueillies au cours d'une période antérieure de 5 à 10 ans.

L'emploi de chiffres de mortalité pour rendre compte quantitativement de l'activité de la grippe est un procédé relativement sommaire; il apparaît cependant qu'en l'absence de données cliniques quantitatives plus précises, l'étude de la surmortalité due aux maladies respiratoires apporte une contribution utile aux recherches épidémiologiques.

Les courbes de mortalité saisonnière prévue permettent une appréciation visuelle rapide de l'activité de la grippe. L'emploi d'échelles variables facilite la comparaison immédiate de cette activité dans plusieurs pays même si les nombres réels de décès enregistrés dans chacun d'eux présentent de fortes différences.

On a affirmé que la surmortalité globale pourrait fournir un meilleur indice de l'intensité des épidémies grippales. La présente étude fait cependant ressortir quelques discordances entre la mortalité par maladies respiratoires et la mortalité globale. De plus, bien que basées sur des chiffres absolus, les courbes n'autorisent qu'une comparaison visuelle entre l'accroissement relatif du nombre des décès enregistrés et celui des décès escomptés. Etant donné que le nombre des décès dus à l'ensemble des causes est de loin supérieur à celui des décès par maladies respiratoires, les déviations par rapport à la courbe de mortalité prévue sont proportionnellement moindres et l'interprétation des graphiques en est rendue plus difficile. Il semble donc plus judicieux, pour le moment, d'utiliser la surmortalité due aux maladies respiratoires.

L'étude collective fournit hebdomadairement des données sur la mortalité par maladies respiratoires aiguës et une analyse rétrospective de la situation épidémiologique dans les pays participants. Elle sera poursuivie pendant plusieurs années apportant des renseignements utiles aux pays intéressés et permettant des comparaisons intéressantes entre pays à climats différents.

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